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ORIGINAL ARTICLE

Herbicidal activity and bioactive components of *Brucea javanica* (L.) Merr. residue

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Abstract There are many nutrients and active substances in the residue of traditional Chinese medicine, which can be processed into organic fertilizer and returned to the field to improve the soil fertility. In this study, we found that *Brucea javanica* (L.) Merr. residue has herbicidal activity and can be used for weed control in the field, this prompted us to investigate the active constituents in it. The herbicidal activities of extracts of *B. javanica* residue were evaluated by conducting bioassays against gramineous weed, *Eleusine indica* (L.) Gaertn. and broad-leaved weed, *Bidens pilosa* L., respectively. It confirmed that ethyl acetate and n-butanol extracts possessed potent biological activities on seed germination and seedling growth of *E. indica* at 5 mg/mL. This prompted us to investigate the active constituents in the seeds residue. By the activity-guided fractionation, eight known compounds were isolated, which were bruceines D–F (**1**–**3**), pityriacitrin (**4**), 4-(9*H*-*β*-carbolin-1-yl)-4-oxobut-2-enoic acid methyl ester (**5**), protocatechuic acid (**6**), vanillic acid (**7**) and carisphthalate (**8**). Then, three quassinoids (**1**–**3**) were evaluated for their potential herbicidal effects in bioassay. Results showed that bruceines D–F have potential herbicidal activity against the test weeds. In the range of experimental concentration, bruceine D had obvious herbicidal effect on the two tested weeds. At the concentration of 31.25 μg/mL, bruceine D could completely inhibit the root growth of *E. indica*; at the concentration of 125 μg/mL, bruceine D can inhibit the seed germination and shoot elongation of *E. indica* and the shoot growth of *B. pilosa*, with the inhibition

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reached 100%. In addition, at the same concentration (250 μg/mL), bruceines D−F could completely affected shoot elongation of *B. pilosa*. These results showed that *B. javanica* residue is a potential source of botanical herbicide development, which has great agricultural economic value, at the same time, the reuse of *B. javanica* residue realizes the transformation of waste into treasure, rational utilization of resources and sustainable development.

1. Introduction

Weeds do serious harm to farmland, affect crop yield and bring huge economic losses (Araniti et al., 2015; Jabran et al., 2015), so weed control is very necessary. At present, the application of chemical herbicides is the main means of weed control, but the widespread use of chemical herbicides has brought negative effects on the environment and human health (Böcker et al., 2019), and also made weeds resistant (Jabran et al., 2015; Ahmed, 2018). Therefore, effective and low toxic weed control methods are urgently needed.

The residues of traditional Chinese herbal medicine produced by the development and utilization of Chinese herbal medicine have been increasing. Among them, the production of Chinese patent medicine brings the largest amount of waste residue, accounting for about 70% of the total amount of drug residue (Yang et al., 2015). Currently, traditional methods of incineration, landfill and stacking in fixed area are often used to treat the herb residues, causing direct or potential damage to the natural environment (Li et al., 2010). Moreover, the waste residue of traditional Chinese medicine still contains high economic value components (Zhao et al., 2012), which can not be reasonably developed and reused, resulting in waste of resources. Therefore, it is of great significance to protect the ecological environment how to effectively utilize the waste of traditional Chinese medicine and realize the transformation of waste into treasure. Recently, the research on the reuse of traditional Chinese medicine residue value is mainly in the direction of agriculture, planting and breeding. For example, it is used for nursery and cultivation substrates, livestock feed production, cultivation of edible fungi, etc (Yang et al., 2015; Xu et al., 2009).

Brucea javanica (L.) Merr. (Ya-dan-zi in Chinese) is a traditional Chinese herbal medicine in China, and the *B. javanica* oil extracted from seeds has a variety of pharmaceutical activities (Cui et al., 2010; Kim et al., 2004). Meanwhile, *B. javanica* oil emulsion is a first-line anti-cancer drug in China (Zhang et al., 2018). However, the waste residue of *B. javanica* produced after oil extraction is rarely reprocessed, resulting in a huge waste of this resource. In addition, the current research on *B. javanica* residue has medical activity (anti-tumor and anti-inflammatory) (Yan et al., 2019; Gao et al., 2019) and agricultural insecticidal activity (Mao et al., 2019), with little herbicidal activity. Moreover, *B. javanica* residue still contains a large number of quassinoid compounds (Wang, 2016), which have phytotoxicity (Heisey and Putnam, 1985). Therefore, the extract of *B. javanica* residue may be a potential source of botanical herbicides.

The purpose of our study is to explore the herbicidal effect of *B. javanica* residue and the possibility of its application in field weed control. Hence, the herbicidal activities of *B. javanica* residue extracts againet two common weeds (*Eleusine indica* (L.) Gaertn. and *Bidens pilosa* L.) in upland crop fields of Guangxi in laboratory and greenhouse conditions were determined. Meanwhile, the inhibitory effects of active compounds on weeds were also surveyed.

2. Materials and methods

2.1. General experimental information

Nuclear magnetic resonance (NMR) spectra were recorded on a Bruker AVANCE III HD 600 Ultra Shield spectrometer (Zurich, Swiss) and calibrated with the residual undeuterated solvent as internal reference. QTOF-MS spectra were acquired on a high-resolution quadrupole time-of-flight (QTOF-MS) system (Xevo G2-S, Waters Corporation, Manchester, UK). Silica gel (100–200, 200–300 mesh) was purchased from Qingdao Marine Chemical Co., Ltd. (Qingdao, China) and Sephadex LH-20 was obtained from GE Healthcare Bio-Sciences AB (Uppsala, Sweden). Rapid medium pressure purification and preparative chromatography CHEETAHMP200 FS-9200S was purchased from Tianjin Agela Technologies Co., Ltd. (Tianjin, China). The other chemicals used in the experiments were of analytical grade. Petroleum ether, ethyl acetate, chloroform, methanol and n-butanol were obtained from Chengdu Kelong Chemical Reagent Factory (Chengdu, China). TLC was performed on silica gel plates GF_{254} (25 × 75 mm) (Qingdao, China). Spots on TLC were visualized under UV light (254 or 365 nm) or by spraying with 10% sulphuric acid in 90% ethanol followed by heating.

2.2. Plant material and weed seeds

The dried seeds of *B. javanica* were collected at Tianlin County, Guangxi Province, People's Republic of China, in September 2019. An authenticated voucher specimen (No. YT2019003) has been deposited at the herbarium of the Agriculture, Guangxi University, Nanning, People's Republic of China. Seeds of *Eleusine indica* (L.) Gaerth. and *Bidens pilosa* L. were collected in Guangxi University farm from September to November 2019. Voucher specimens were deposited in the herbarium of the Agriculture, Guangxi University (GXU201909-EI and GXU201909-BP).

2.3. Extraction procedures

In this study, we mainly discussed the herbicidal activity of *B. javanica* residue and its possibility in weed control. Therefore, we refer to the methods reported in the previous literature (Kim et al., 2016) and make corresponding improvements in

the pretreatment of *B. javanica* seeds. The dried *B. javanica* seeds were crushed by a grinder to obtain powder of *B. javanica* seeds (10 kg), then used to extract oil, and then the residues left after oil extraction were ultrasonically extracted three times with methanol at room temperature. The extract solution was concentrated with a rotary evaporator (54 °C) under reduced pressure to give a dried extract. Then the methanolic extract (M, 2 kg) was dissolved in water and made into suspension (20 L). The suspension was first degreased with petroleum ether. Then, the degreased material was extracted sequentially with ethyl acetate and n-butanol. The extracts were evaporated under vacuum to produce the corresponding fractions of petroleum ether extract (PE, 495 g), ethyl acetate extract (EA, 66 g) and n-butanol extract (n-B, 198 g). The crude extracts were naturally cooled to room temperature, then sealed with preservative film and stored in the refrigerator at −20 °C for subsequent experiments.

2.4. Laboratory herbicidal activity assay

According to Petri dish filter paper method reported by Kaab et al. (2020), it has been improved. Seeds of *E. indica* as a model of gramineous weed and *B. pilosa* as a model of broad-leaved weed were sterilised using 10% sodium hypochlorite for 20 min, and then washed three times with sterile deionized water. Crude extracts or compounds were first fully dissolved in methanol (the volume ratio of methanol to the solvent does not exceed 5%), and then diluted to the required concentration with deionized water. Two layers of filter paper [placed on the bottom of the inverted Petri dish (90 × 15 mm) cover] were moistened with 2 mL solution of different concentrations, and then thirty sterilized weed seeds (arranged by 5 × 6) were immediately placed in each Petri dish, and finally 3 mL solution was added. At the same time, the negative control (solvent control) and blank control with the same volume ratio were set up, and each treatment was repeated for three times. After treatment, all Petri dishes were transferred to constant temperature incubator (temperature: 30 ± 2 °C, relative humidity: 75%, light/dark: 14/10 h) for culture. During cultivation, an appropriate amount of deionized water was added to maintain the water required for seed growth. The condition of seed germination was observed every day, and the number of seed germination was recorded for 7 days. After 7 days, the germination number of seeds (root protrusion of 1–2 mm) was counted, the root length and shoot length of germinated seeds were measured, and the inhibition rates were calculated according to equation (1), in which C represents parameters of the negative control group and T represents parameters of the treatment group.

$$\text{Inhibition rate } (\%) = (C - T)/C \times 100 \quad (1)$$

2.5. Greenhouse herbicidal activity assay

The pre-emergent herbicidal activity of extracts against *E. indica* and *B. pilosa* was evaluated using pot culture assay (Ma et al., 2018). The specific experimental process has made some changes on the basis of literature reports. Firstly, all the 200 mL disposable plastic cups (3 holes were made at the bottom of the cup with an electric melting gun) were filled with 150 g breeding medium (substrate/sand/clay, v/v/v 1:1:1), then the mixture wetted with 25 mL of water. Ten weed seeds (arranged in 3 × 4 × 3) were placed in each plastic cup, and the seeds were covered with a layer of fine sand. Finally, 25 mL of different concentrations of test solution (prepared by dissolving the extracts in methanol and then diluted with deionized water to final concentrations) were added. At the same time, the solvent control and blank control with the same volume ratio were set up, and each treatment was repeated for three times. After treatment, the self-made breeding pots were placed in greenhouse (temperature: 25 ± 2 °C, relative humidity: 75%, natural light) for cultivation. During the cultivation period, appropriate amount of corresponding test solution should be added to maintain the water needed for seed growth. The emergence of seeds was observed and the emergence number of seeds was recorded every day. The observation lasted for 30 days. After 15 days, the seed emergence inhibition rate was calculated by equation (1).

2.6. Isolation of compounds

The BuOH extract was subjected to column chromatography (CC) on silica gel (100–200 mesh), eluted with ethyl acetate–methanol (v/v 100:0–0:100) to give 7 fractions (F1-F7). Fraction F1 (14.5 g) was separated by CC on silica gel (0 to 20% methanol in chloroform) furnishing 5 sub-fractions (F1.1-F1.5). Sub-fraction F1.1 (3.8 g) was purified by the rapid medium pressure preparation system in gradient elution of ethyl acetate–methanol and recrystallization in acetone solvent to provide compound **1** (320 mg). Sub-fractions F1.4 (1.7 g) was separated by the rapid medium pressure preparation system (petroleum ether-ethyl acetate and ethyl acetate–methanol) to afford 7 subfractions. The fourth subfraction (F1.4.4, 0.2 g) was purified twice by silica gel CC and then on a Sephadex LH-20 column ($CHCl_3$/MeOH: 1/1), yielding compound **4** (6.6 mg). Sub-fractions F1.5 (2.9 g) was further purified by repeated silica gel CC and the rapid medium pressure preparation system, finally purified with a Sephadex LH-20 column with chloroform/methanol (1/1) to yield pure compound **8** (15 mg). Sub-fractions F1.2 (4.1 g) was subjected to the rapid medium pressure preparation system in gradient elution of petroleum ether/ethyl acetate and ethyl acetate/methanol then led to 8 subfractions. The third subfraction (F1.2.3, 1.1 g) was further isolated by silica gel CC and Sephadex LH-20 ($CHCl_3$/MeOH: 1/1) to provide compound **5** (6.4 mg). The fourth to seventh subfractions (F1.2.4-F1.2.7, 1.9 g) were combined, and then the combined subfraction was separated by three Sephadex LH-20 elution ($CHCl_3$/MeOH: 1/1, 2×; acetone, 1×) and one silica gel CC purification, respectively, giving compound **6** (11.2 mg). Sub-fractions F1.3 (2.0 g) was separated by the rapid medium pressure preparation system in gradient elution of PE-EtOAc (0–50%) and EtOAc-MeOH (0–20%) into 6 subfractions. The third subfraction (F1.3.3, 500 mg) was separated by repeated Sephadex LH-20 CC (chloroform/methanol: 1/1, 1×; methanol, 1×) and finally purified by silica gel CC, using a gradient of MeOH in $CHCl_3$ (2–10%) for elution, to afford compound **7** (19.1 mg). One hundred milligram crude product (marked as F2″, 100 mg) was taken out and further purified by silica gel CC (gradient elution of $CHCl_3$-MeOH, 10–30%) to obtain compound **2** (87 mg). Fraction F3 (28.4 g) was fractionated using chromatography over a silica gel column and eluted with $CHCl_3$-

MeOH mixtures of increasing polarity (0–50%), getting 6 sub-fractions (F3.1-F3.6). Sub-fraction F3.4 (26.3 g) was separated by the rapid medium pressure preparation system in gradient elution of EtOAc-MeOH (0–50%) and MeOH-H_2O (20–50%), respectively, following recrystallization in acetone solvent, yielding compound **3** (280 mg).

2.7. Structural identification

By the activity-guided fractionation, eight compounds (Fig. 1) were isolated from the n-butanol extract of *B. javanica* residue.

Compound **1** (bruceine D), colorless needle. ^{1}H NMR (600 MHz, CD_3OD): δ 6.06 (1H, dd, J = 3.0, 1.8 Hz, H-3), 5.24 (1H, s, H-15), 5.12 (1H, t, J = 5.4, 3.0 Hz, H-7), 4.61 (1H, d, J = 4.2 Hz, H-11), 4.55 (1H, d, J = 7.8 Hz, H-1), 3.85 (1H, dd, J = 7.8, 1.8 Hz, H-20), 3.77 (1H, d, J = 1.2 Hz, H-12), 2.97 (1H, br. d, J = 12.6 Hz, H-5), 2.42 (1H, dd, J = 4.8, 1.2 Hz, H-9), 2.38 (1H, dt, J = 15.0, 3.0 Hz, H-6α), 1.99 (3H, s, H-17), 1.88 (1H, m, H-6β), 1.44 (3H, s, H-18), 1.19 (3H, s, H-19); ^{13}C NMR (150 MHz, CD_3OD): δ 10.1 (C-19), 17.0 (C-18), 21.1(C-17), 27.3 (C-6), 43.0 (C-5), 44.9 (C-9), 48.2 (C-10), 49.4 (C-8), 69.0 (C-20), 69.3 (C-15), 74.1 (C-11), 79.7 (C-7), 80.0 (C-12), 81.0 (C-14), 81.6 (C-1), 83.6 (C-13), 123.8 (C-3), 164.2 (C-4), 174.9 (C-16), 198.5 (C-2). The ^{1}H and ^{13}C NMR data were in accordance with those of bruceine D (NoorShahida et al., 2009).

Compound **2** (bruceine E), colorless needles. ^{1}H NMR (600 MHz, CD_3OD): δ 5.41 (1H, d, J = 1.8 Hz, H-3), 5.15 (1H, s, H-15), 5.08 (1H, t, J = 5.4, 2.4 Hz, H-7), 4.64 (1H, d, J = 7.2 Hz, H-11), 4.01 (1H, m, H-1), 3.84 (1H, dd, J = 7.2, 1.2 Hz, H-20), 3.77 (1H, d, J = 0.6 Hz, H-12), 2.43 (1H, d, J = 12.6 Hz, H-5), 2.18 (1H, dt, J = 15.0, 3.0 Hz, H-6), 2.09 (1H, d, J = 3.6 Hz, H-9), 1.74 (1H, dd, J = 13.2, 1.2 Hz, H-6), 1.67 (3H, d, J = 12.6 Hz, H-17), 1.43 (3H, s, H-18), 1.24 (3H, s, H-19); ^{13}C NMR (150 MHz, CD_3OD): δ 10.8 (C-19), 17.0 (C-18), 19.7 (C-17), 27.2 (C-6), 42.4 (C-5), 44.0 (C-10), 45.3 (C-9), 49.6 (C-8), 69.2 (C-20), 69.4 (C-15), 72.8 (C-2), 74.4 (C-11), 79.8 (C-7), 80.6 (C-12), 81.0 (C-14), 81.4 (C-1), 83.4 (C-13), 123.8 (C-3), 135.2 (C-4), 175.1 (C-16). The ^{1}H and ^{13}C NMR data were in accordance with those of bruceine E (NoorShahida et al., 2009).

Compound **3** (bruceine F), colorless needles. ^{1}H NMR (600 MHz, DMSO d_6): δ 5.31 (1H, s, H-3), 4.88 (2H, m, H-1, H-7), 4.46 (1H, d, J = 7.2 Hz, H-20), 4.38 (1H, t, J = 10.8, 5.4 Hz, H-12), 3.95 (1H, m, H-18), 3.81 (1H, s, H-15), 3.70 (3H, m, H-2, H-18, H-20), 3.39 (1H, m, H-11), 2.27 (1H, d, J = 12.6 Hz, H-5), 1.96 (1H, m, H-6), 1.93 (1H, m, H-9), 1.57(3H, s, H-17), 1.53 (1H, m, H-6), 1.08 (3H, s, H-19); ^{13}C NMR (150 MHz, DMSO d_6): δ 12.1 (C-19), 21.2 (C-17), 27.6 (C-6), 42.3 (C-5), 44.2 (C-10), 44.9 (C-9), 49.7 (C-8), 62.8 (C-18), 69.3 (C-7), 69.8 (C-20), 72.4 (C-15), 74.4 (C-12), 75.9 (C-2), 79.3 (C-1), 81.6 (C-11), 82.5 (C-14), 83.5 (C-13), 125.7 (C-3), 134.1 (C-4), 174.2 (C-16). The ^{1}H and ^{13}C NMR data were in accordance with those of bruceine F (Li and Zuo, 1980).

Compound **4** (pityriacitrin), yellow feathery microcrystalline. QTOF-ESI-MS m/z 312.1235 $[M + H]^+$ (calcd for $C_{20}H_{13}N_3O$). ^{1}H NMR (600 MHz, $CDCl_3$): δ 9.48 (1H, d, J = 3.0 Hz, H-2′), 8.60 (1H, d, J = 4.8 Hz, H-3), 8.21 (1H, br. dd, J = 7.8, 0.6 Hz, H-5), 8.18 (1H, d, J = 4.8 Hz, H-4), 7.64 (1H, m, H-7), 7.64 (1H, m, H-8), 7.52 (1H, d, J = 7.8 Hz, H-7′), 7.43 (1H, m, H-5′), 7.38 (1H, m, H-6), 7.34 (1H, m, H-6′); ^{13}C NMR (150 MHz, $CDCl_3$): δ 111.3 (C-7′), 112.0 (C-8), 115.9 (C-3′), 117.8 (C-4), 120.4 (C-6), 120.9 (C-5a), 121.8 (C-5), 122.7 (C-4′), 122.9 (C-5′), 123.7 (C-6′), 127.5 (C-3a′), 129.0 (C-7), 131.5 (C-4a), 135.5 (C-7a′), 136.6 (C-9a), 136.8 (C-3), 137.5 (C-2′), 138.3 (C-1), 141.1 (C-8a), 189.0 (C-10). The ^{1}H and ^{13}C NMR data were in accordance with those of pityriacitrin (Mayser et al., 2002) isolated from the yeast *Malassezia furfur*. This compound has been reported as a secondary metabolite of marine bacteria and synthetic compound (Zhang et al., 2011) in previous studies.

Compound **5** [4-(9*H*-β-carbolin-1-yl)-4-oxobut-2-enoic acid methyl ester], yellow green solid. QTOF-ESI-MS m/z 281.0940 $[M + H]^+$ (calcd for $C_{16}H_{12}N_2O_3$). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.85 (1H, d, J = 16.2 Hz, H-11), 8.64 (1H, d, J = 4.8 Hz, H-3), 8.23 (1H, br. dd, J = 4.8, 0.6 Hz, H-4), 8.21 (1H, br. dd, J = 7.8, 0.6 Hz, H-5), 7.67 (1H, m, H-8), 7.62 (1H, m, H-7), 7.40 (1H, m, H-6), 7.13 (1H, d, J = 15.6 Hz, H-12), 3.91 (3H, s, H-14); ^{13}C NMR (150 MHz, $CDCl_3$): δ 52.3 (C-14), 112.1 (C-8), 119.8 (C-4), 120.7 (C-5a), 121.1 (C-6), 122.0 (C-6), 129.5 (C-7), 131.4 (C-12), 131.8 (C-4a), 135.5 (C-1), 135.9 (C-9a), 136.5 (C-11), 138.7 (C-3), 141.1 (C-8a), 166.2 (C-13), 191.2 (C-10). The ^{1}H and ^{13}C NMR data were in accordance with those of 4-(9*H*-β-carbolin-1-yl)-4-oxobut-2-enoic acid methyl ester, previously isolated from terrestrial *Streptomycetes* (Fotso et al., 2008) and the rhizomes of *Polygonatum sibiricum* Red. (Zhao et al., 2018).

Compound **6** (protocatechuic acid), colorless needle. ^{1}H NMR (600 MHz, CD_3OD): δ 7.46 (1H, m, H-2), 7.44 (1H, m, H-6), 6.83 (1H, d, J = 7.8 Hz, H-5); ^{13}C NMR (150 MHz, CD_3OD): δ 114.4 (C-5), 116.3 (C-2), 121.7 (C-6), 122.5 (C-1), 144.7 (C-3), 150.1 (C-4), 168.9 (HOOC-1′). The ^{1}H and ^{13}C NMR data were in accordance with those of protocatechuic acid (Colombo et al., 2010).

Compound **7** (vanillic acid), colorless solid. ^{1}H NMR (600 MHz, CD_3OD): δ 7.58 (1H, m, H-2), 7.57 (1H, m, H-6), 6.86 (1H, d, J = 9.0 Hz, H-5), 3.91 (3H, s, H_3CO-3); ^{13}C NMR (150 MHz, CD_3OD): δ 55.0 (H_3CO-3), 112.4 (C-2), 114.4 (C-5), 123.9 (C-1), 147.3 (C-3), 151.3 (C-4), 168.1 (HOOC-1′). The ^{1}H and ^{13}C NMR data were in accordance with those of vanillic acid (Colombo et al., 2010).

Compound **8** (carisphthalate), white crystalline solid. QTOF-ESI-MS m/z 577.1328 $[M + H]^+$ (calcd for $C_{30}H_{24}O_{12}$). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.13 (12H, s, H-2, 3, 5, 6, 2″, 3″, 5″, 6″, 2‴, 3‴, 5‴, 6‴), 4.69 (12H, s, H-1′, 2′, 1‴, 2‴, 1⁗, 2⁗); ^{13}C NMR (150 MHz, $CDCl_3$): δ 62.8 (C-1′, 2′, 1‴, 2‴, 1⁗, 2⁗), 129.8 (C-2, 3, 5, 6, 2″, 3″, 5″, 6″, 2‴, 3‴, 5‴, 6‴), 133.8 (C-1, 4, 1″, 4″, 1‴, 4‴), 165.3 (C-7, 8, 7″, 8″, 7‴, 8‴). The above data were basically consistent with the spectral data of carisphthalate isolated from the methanol extract of *Carissa opaca* (Parveen et al., 2017) or the marine-derived actinomycetes *Streptomyces* sp. G278 (Cao et al., 2018). In addition, the compound was previously reported as a synthetic derivative (Kint et al., 2003).

2.8. Statistical analyses

The results were presented as mean and standard deviation of all replicates. An one-way analysis of variance (ANOVA) was used to determine whether there were significant ($p < 0.05$)

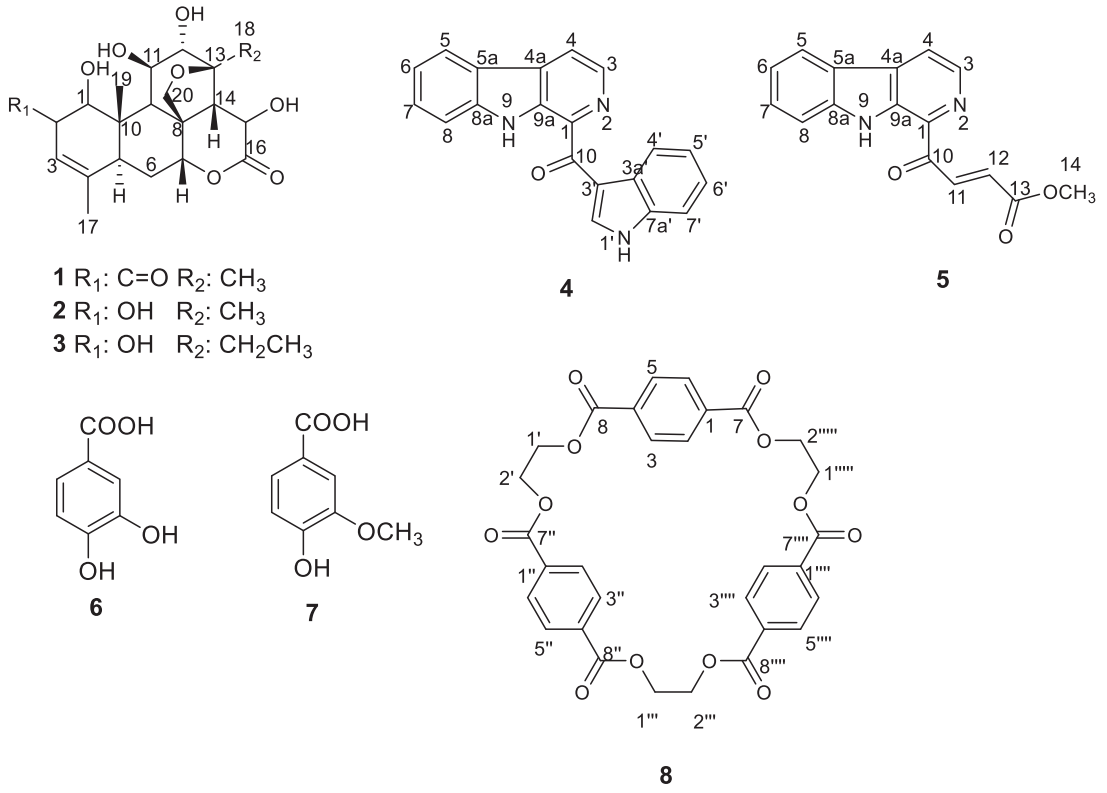

Fig. 1 Chemical structures of compounds **1**–**8**.

treatment effects between groups, and the means were compared using Duncan's multiple range test (DMRT).

3. Results

*3.1. Herbicidal activity of **B. javanica** extracts in laboratory*

The herbicidal activities of organic extracts of *B. javanica* residue on seed germination and seedling growth (root and shoot elongation) of *E. indica* and *B. pilosa* in laboratory were investigated (Table 1). The inhibitory effects on *E. indica* and *B. pilosa* at 10 mg/mL (methanol extract) and 5 mg/mL (petroleum ether, ethyl acetate and n-butanol extract) on germination and seedling growth varied significantly. Both ethyl acetate and n-butanol extracts of *B. javanica* residue completely suppressed germination of *E. indica* seeds. In addition, ethyl acetate extract also showed excellent inhibitory effect against seed germination of *B. pilosa*, while the methanolic extract showed a good inhibitory activity on the germination of *E. indica* and *B. pilosa*, with inhabition of 84.08% and 60.65%, respectively.

However, root elongation was essentially remarkably restrained for extracts of *B. javanica* (Fig. 2). At 10 mg/mL, methanol crude extract showed significant inhibitory activity against root growth of *E. indica* and *B. pilosa*. At 5 mg/mL, ethyl acetate and n-butanol extracts completely inhibited the seedling growth of *E. indica*. Similarly, ethyl acetate extract and n-butanol extract also had significant effect on the root length of *B. pilosa*.

On the other hand, the shoot growth of *E. indica* and *B. pilosa* were also severely inhibited by the extracts (Fig. 2). At the same concentration (5 mg/mL), the shoot elongation of *E. indica* was completely affected by ethyl acetate and n-butanol extracts. Moreover, methanol extract, ethyl acetate extract and n-butanol extract could completely prevent the shoot growth of *B. pilosa* under the corresponding concentrations.

3.2. Herbicidal activity of B. javanica extracts under greenhouse conditions

The inhibitory effect of the tested extracts on emergence of *E. indica* and *B. pilosa* 15 d after treatment (Table 2 and Fig. 3). The methanol, ethyl acetate and n-butanol extracts strongly inhibited the emergence of these two weeds at the corresponding tested concentrations. Remarkably, n-butanol extract completely inhibited on emergence of *E. indica* and *B. pilosa*. However, methanol and ethyl acetate extracts only inhibited the emergence of *E. indica* completely.

After 30 days of pot experiment, the effect of different extracts on the growth of seedlings of *B. pilosa* changed significantly (Fig. 3). Compared with the results of 15 days investigation, the n-butanol extract of *B. javanica* not only completely inhibited the emergence of *B. pilosa*, but also inhibited its growth. However, methanol extract and ethyl acetate extract had some inhibition on the emergence of *B. pilosa*, but the inhibition on the growth of seedlings is weak, and they were weaker than n-butanol extract.

3.3. Structural elucidation

The bioassay-guided separation of the components in the n-butanol extract of *B. javanica* residue revealed eight chemical constituents. All the compounds were purified by column chro-

Table 1 Effect of *B. javanica* extracts on seed germination of *E. indica* and *B. pilosa* in laboratory[a] (7 d).

Treatments	Conc. (mg/mL)	*E. indica*		*B. pilosa*	
		Seed germination	Inhibition rate (%)	Seed germination	Inhibition rate (%)
Blank[b]	–	25.00 ± 0.65	–	28.00 ± 0.35	–
CK[c]	–	27.75 ± 0.31	–	29.00 ± 0.29	–
M	10	4.50 ± 0.75	84.08 ± 2.59	11.50 ± 1.01	60.65 ± 3.19
PE	5	23.75 ± 1.11a	14.74 ± 3.25b	22.50 ± 0.32a	22.44 ± 0.55c
EA	5	0.00 ± 0.00b	100.00 ± 0.00a	3.50 ± 0.43c	88.04 ± 1.44a
n-B	5	0.00 ± 0.00b	100.00 ± 0.00a	17.25 ± 1.03b	40.77 ± 3.13b

[a] Data represent the mean ± SE, n = 3. Different lowercase letters in a column indicate that the means are significantly different at $p < 0.05$ based on Duncan's multiple range test (DMRT).
[b] Blank control.
[c] Negative control.

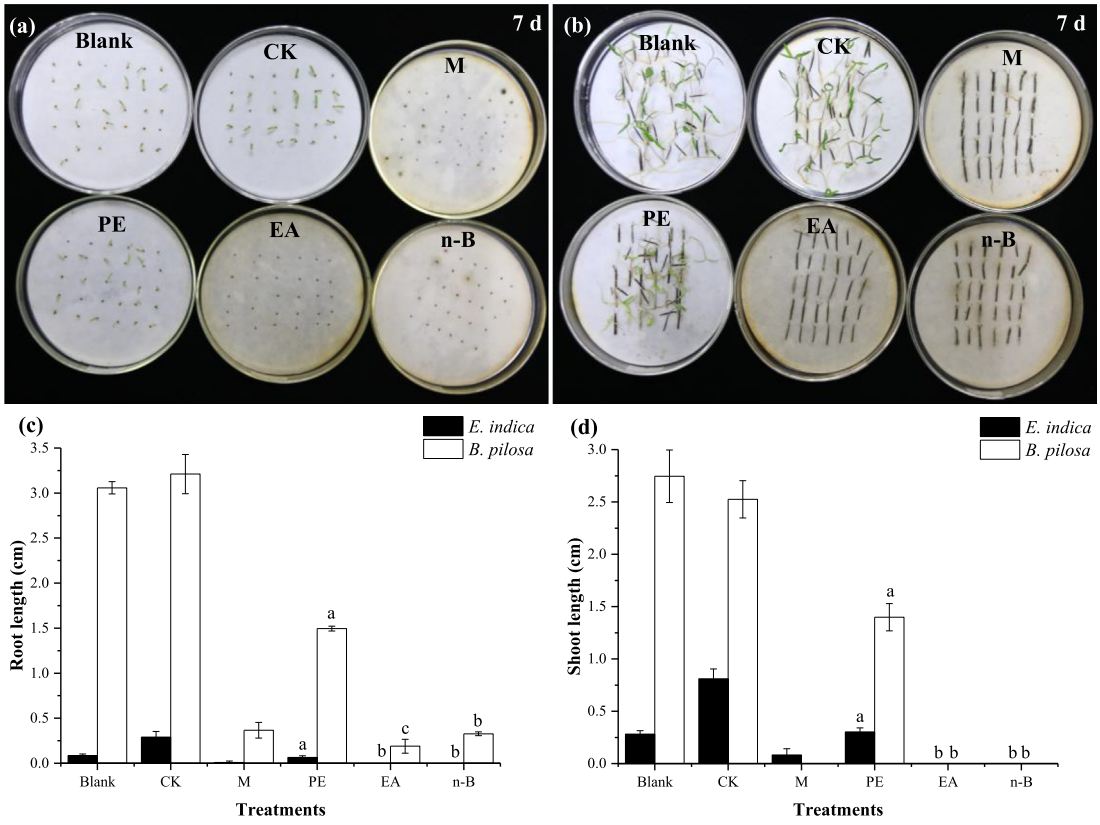

Fig. 2 Effect of organic extracts of *B. javanica* on *E. indica* (a) and *B. pilosa* (b). Effect of *B. javanica* extracts on the root (c) and shoot (d) length of *E. indica* and *B. pilosa*. The data in the figure were given as mean ± SD for three repetitions. Different letters indicated significantly different ($p < 0.05$) among the columns with same color, based on DMRT. (Blank: blank control; CK: negative control; M: methanol extract, 10 mg/mL; PE: petroleum ether extract, EA: ethyl acetate extract, n-B: n-butanol extract, 5 mg/mL).

matography, and their structures were characterized by ^{1}H NMR, ^{13}C NMR and ESI-MS. Additionally, their structures were confirmed by direct comparisons with previously reported spectroscopic data (NoorShahida et al., 2009; Li and Zuo, 1980; Mayser et al., 2002; Fotso et al., 2008; Colombo et al., 2010; Parveen et al., 2017). On the basis of the spectroscopic data, the constituents were identified as the known compounds, bruceine D (**1**), bruceine E (**2**), bruceine F (**3**), pityriacitrin (**4**), 4-(9*H*-*β*-carbolin-1-yl)-4-oxobut-2-enoic acid methyl ester (**5**), protocatechuic acid (**6**), vanillic acid (**7**) and carisphthalate (**8**). Among them, pityriacitrin, 4-(9*H*-*β*-carbolin-1-yl)-4-oxobut-2-enoic acid methyl ester and carisphthalate were isolated from *B. javanica* residue for the first time.

3.4. Herbicidal activity of three quassinoid compounds

The laboratory herbicidal activities of compounds bruceines D–F (**1**–**3**) were evaluated using *E. indica* and *B. pilosa* at 250 μg/mL. In the herbicidal activity assay, all of the three

Table 2 Effect of *B. javanica* extracts on emergence of *E. indica* and *B. pilosa* under greenhouse conditions[a] (15 d).

Treatments	Conc. (mg/mL)	*E. indica*		*B. pilosa*	
		Seedling emergence	Inhibition rate (%)	Seedling emergence	Inhibition rate (%)
M	10	0.00 ± 0.00	100.00 ± 0.00	1.00 ± 0.20	86.61 ± 2.56
PE	5	1.75 ± 0.13a	63.75 ± 1.88b	4.25 ± 0.24a	33.48 ± 2.04b
EA	5	0.00 ± 0.00b	100.00 ± 0.00a	0.25 ± 0.13b	96.88 ± 1.56a
n-B	5	0.00 ± 0.00b	100.00 ± 0.00a	0.00 ± 0.00b	100.00 ± 0.00a

[a] Data represent the mean ± SE, n = 3. Different lowercase letters in a column indicate that the means are significantly different at $p < 0.05$ based on Duncan's multiple range test (DMRT).

quassinoid compounds exhibited potential inhibition against the seed germination of *E. indica* with inhibition of 100.00%, 43.29% and 49.96%, respectively (Table 3). At this concentration, bruceine D showed the greatest germination inhibition in *E. indica*, which was far stronger than atrazine (−4.82%), a commercial herbicide co-assayed as the positive control. Conversely, bruceine D had weaker inhibitory activity against the seed germination of *B. pilosa*, but the inhibitory rate (46.67%) was much greater than those of atrazine (10.00%). However, the inhibition of bruceine E and F on seed germination of *B. pilosa* was very weak or not at all.

Furthermore, bruceine D, E and F could significantly affected seedling growth of these two weeds. The 7-day investigation results (Fig. 4) showed that bruceine D represented the strongest inhibitory effect on seedling growth of *E. indica* and the root elongation of *B. pilosa* at 250 μg/mL compared with atrazine and the negative control. Further, the shoot elongation of *B. pilosa* was also completely suppressed at this concentration for bruceine E and F.

The herbicidal effect of bruceine D at different concentrations (31.25, 62.5, 125, 250, 500 μg/mL) was further determined (Fig. 5). Bruceine D showed significant inhibitory effect on seed germination and growth of *E. indica* in the range of experimental concentrations, and which was far stronger than that of positive control. In particular, bruceine D completely inhibit root growth of *E. indica* at concentrations as low as 31.25 μg/mL, while it caused complete inhibition of seed germination and shoot elongation of *E. indica* when the concentration was at least 125 μg/mL. Furthermore, bruceine D also completely suppressed the shoot growth of *B. pilosa* at a concentration of 125 μg/mL. However, the inhibitory effect of bruceine D on the germination of *B. pilosa* seeds was the greatest when the concentration reached the maximum.

4. Discussion

In this study, the methanol, ethyl acetate and n-butanol extracts of *B. javanica* residue had certain inhibitory effects on the gramineous weed (*E. indica*) and the broad-leaved weed (*B. pilosa*). In particular, ethyl acetate and n-butanol extracts showed the most significant inhibition on seed germination and growth of *E. indica*. These results indicated that *B. javanica* residue has potential herbicidal activity, which are consistent with the previous reports (Wang, 2016; Heisey and Putnam, 1985). It has been previously reported that there are still a large number of chemical components with high activity in the residues produced after the extraction of *B. javanica* oil, among which the content of quassinoids is relatively high (Wang, 2016). In addition, quassinoid compounds have phytotoxicity (Heisey and Putnam, 1985).

The total amount of plant residues, especially waste residue of medicinal plants (i.e. herbal residues) is huge. If it is not handled properly, it will cause waste of resources and environmental pollution (Li et al., 2010). At present, there are many ways to utilize traditional herbal residues as resources (Yang et al., 2015; Xu et al., 2009), which effectively alleviates the situation of difficult comprehensive utilization of herbal residues. Herbal residue is a kind of high quality light substrate raw material and organic fertilizer, which can be used to raise seedlings and cultivate substrates and improve soil fertility. In addition, it can make the seedlings grow and strengthen the disease resistance (Yang et al., 2015). Therefore, the residues of *B. javanica* seed can be processed into organic fertilizer to improve the field fertility, improve the utilization efficiency of the waste resource, turn the waste into treasure, and realize the sustainable development of environment and agriculture.

Weeds reduce the yield and quality of crops (Jabran et al., 2015), so weed control is imminent. Currently, the application of chemical herbicides is still the main means of weed control (Böcker et al., 2019), but its limitations urge us to find new efficient and low toxic weed control methods. In recent years, the plant crude extract with herbicidal activity has gradually become a research hotspot. The reasons are as follows: on the one hand, it is the basis of separating and identifying high herbicidal activity compounds and developing botanical herbicides; on the other hand, many plant crude extracts can be directly applied to weed control in the field. The crude extracts of many plants can severely inhibit seed germination and growth of weeds. Theoretically, this preparation can be used as a natural herbicide (Duke et al., 2002; Yang, 2008). Therefore, *B. javanica* waste residue can be used to control of weeds in the field, especially for the control of grass weeds, because of its pre-emergent sealing effect on grass weeds, the herbicidal activity is significant. In this study, bruceine D, an active herbicidal compound, was obtained from *B. javanica* residue by activity tracing. In addition, our results indicated that bruceine D can inhibit the seed germination and growth of grass weeds and broad-leaved weeds at a certain concentration, which is expected to be used as a leading compound to develop botanical herbicides.

In previous reports, bruceine D performanced significant anti-cancer activity, which usually inhibited the proliferation of cancer cells or caused apoptosis by regulating some biological processes in cells (Fan et al., 2020; Shen et al., 2020; Tian et al., 2020). In addition, bruceine D also had hypoglycaemic (Choo et al., 2012), anthelmintic (Wang et al., 2011), antibabe-

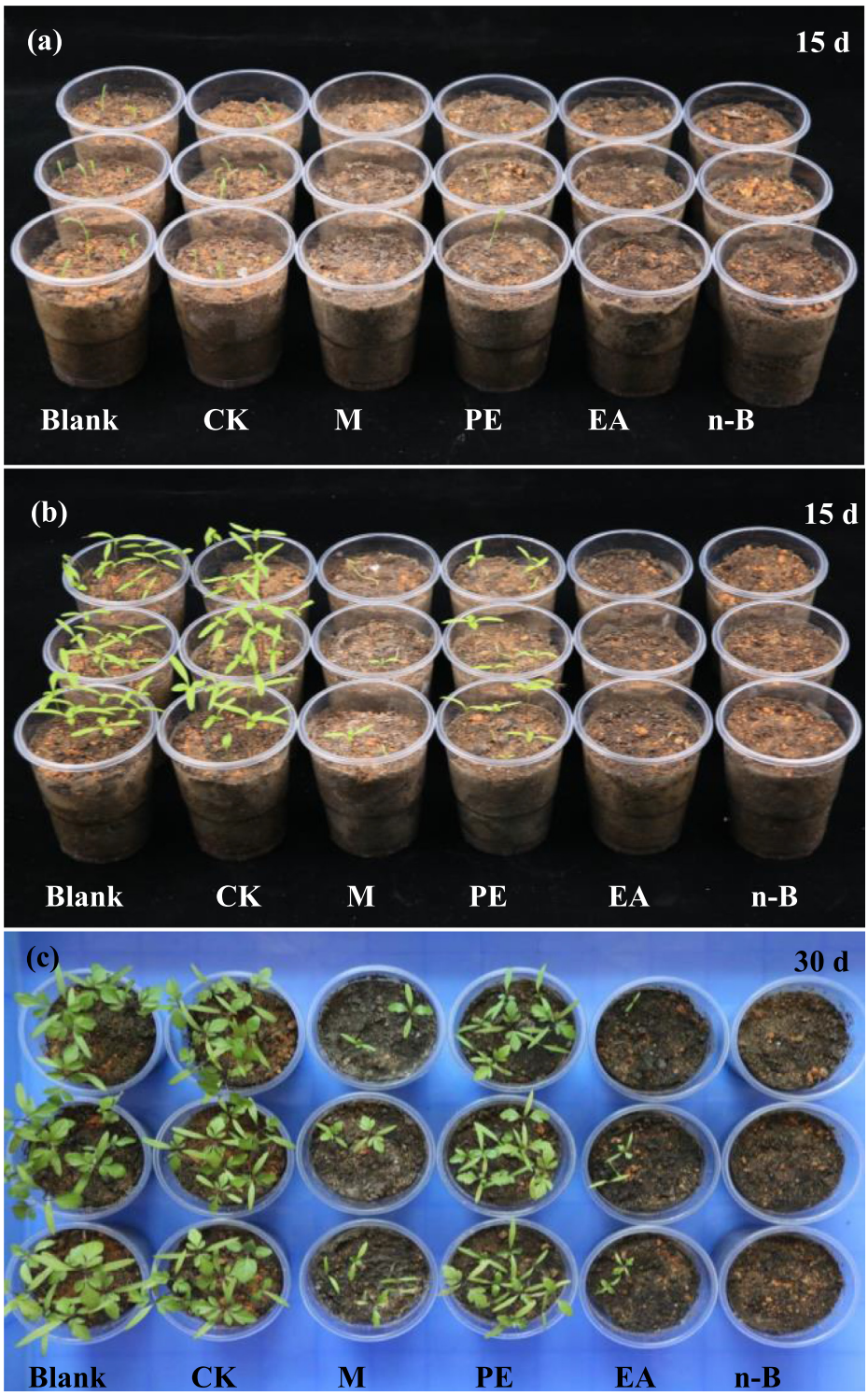

Fig. 3 Effect of organic extracts of *B. javanica* on emergence of *E. indica* (a) and *B. pilosa* (b). Effect of *B. javanica* extracts on the growth of *B. pilosa* (c). (Blank: blank control; CK: negative control; M: methanol extract, 10 mg/mL; PE: petroleum ether extract, EA: ethyl acetate extract, n-B: n-butanol extract, 5 mg/mL).

sial (Subeki et al., 2007) and antitobacco mosaic virus (TMV) activities (Yan et al., 2010). Similarly, bruceine E, which is similar to bruceine D in structure, also has cytotoxic (Liu et al., 2011; Liu et al., 2012) and hypoglycemic activities (Choo et al., 2012). In contrast, there are almost no studies on the activity of bruceine F. Therefore, in the present work, bruceine D, E and F, which were obtained from *B. javanica* residue, exhibited a certain inhibitory effect on *E. indica* and *B. pilosa*. Among them, bruceine D can completely inhibit the root elongation of *E. indica* at 31.25 μg/mL, and can completely inhibit

Table 3 Effects of bruceines D–F on seed germination of *E. indica* and *B. pilosa* in laboratory[a] (7 d).

Treatments	Conc. (μg/mL)	*E. indica*		*B. pilosa*	
		Seed germination	Inhibition rate (%)	Seed germination	Inhibition rate (%)
Blank[b]	–	26.75 ± 0.55	–	29.25 ± 0.13	–
CK[c]	–	26.75 ± 0.38	–	30.00 ± 0.00	–
Atrazine[d]	250	28.00 ± 0.20a	−4.82 ± 0.95c	27.00 ± 0.35a	10.00 ± 1.18b
Bruceine D	250	0.00 ± 0.00c	100.00 ± 0.00a	16.00 ± 0.54b	46.67 ± 1.80a
Bruceine E	250	15.25 ± 0.75b	43.29 ± 2.08b	27.25 ± 0.38a	9.17 ± 1.25b
Bruceine F	250	13.50 ± 1.01b	49.96 ± 3.16b	25.75 ± 0.63a	14.17 ± 2.08b

[a] Data represent the mean ± SE, n = 3. Different lowercase letters in a column indicate that the means are significantly different at $p < 0.05$ based on Duncan's multiple range test (DMRT).
[b] Blank control.
[c] Negative control.
[d] Positive control.

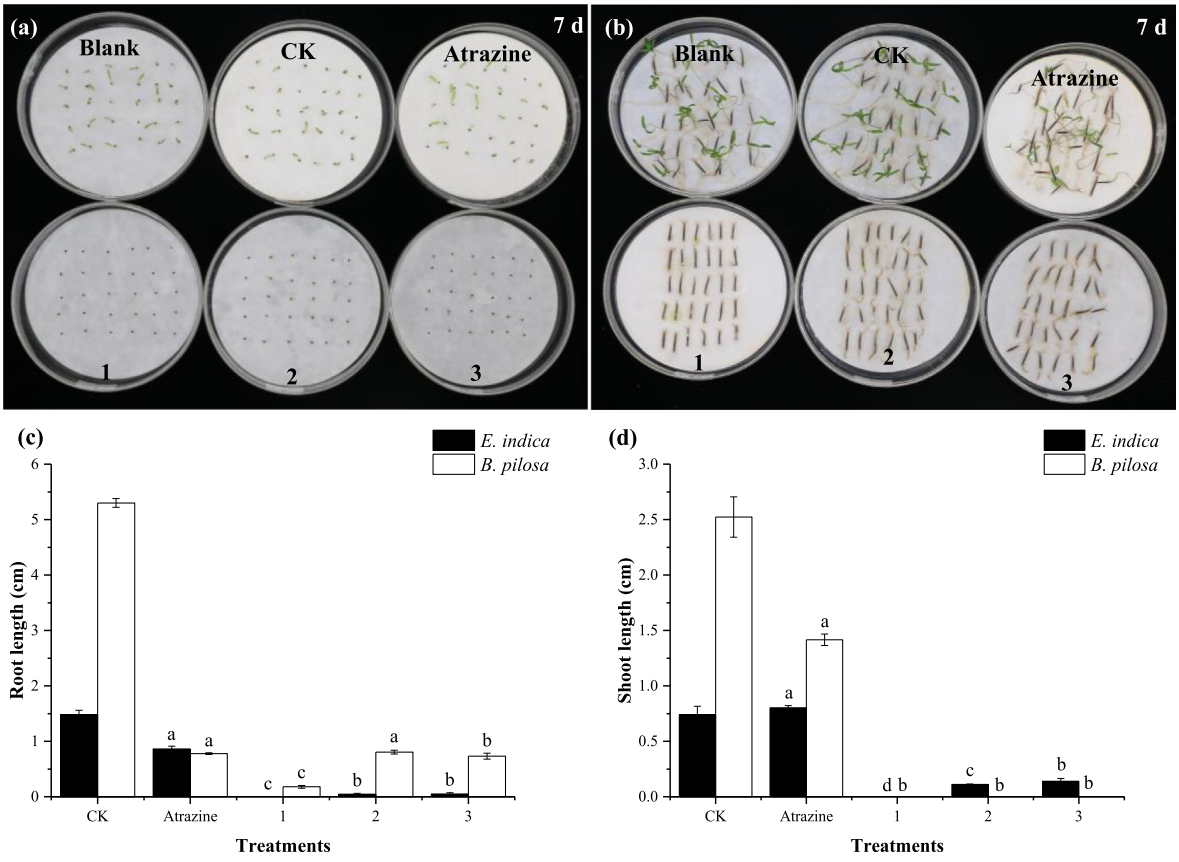

Fig. 4 Effect of bruceines D–F from *B. javanica* on *E. indica* (a) and *B. pilosa* (b). Effect of compounds D–F on the root (c) and shoot (d) length of *E. indica* and *B. pilosa*. The data in the figure were given as mean ± SD for three repetitions. Different letters indicated significantly different ($p < 0.05$) among the columns with same color, based on DMRT. (Blank: blank control; CK: negative control; Atrazine: positive control, **1**: bruceine D, **2**: bruceine E, **3**: bruceine F, 250 μg /mL).

the seed germination and growth of *E. indica* and the shoot elongation of *B. pilosa* at 125 μg/mL. This is similar to the result that bruceine D aqueous solution reported in the invention patent can completely inhibit the seed germination of monocotyledonous weed (*Avena fatua* L.) and dicotyledonous weed (*Brassica napus* L.) at the concentration of 200 and 400 μg/mL, respectively (Li et al., 2016). Therefore, bruceine D can significantly inhibit the germination of weed seeds at a lower concentration. In addition, bruceine E and F can completely inhibit the shoot growth of *B. pilosa* at 250 μg/mL. These results are supported by the phytotoxicity of the previously reported quassinoids (Heisey and Putnam, 1985).

Furthermore, our results showed that the inhibitory effects of bruceines D–F (**1**–**3**) at the same concentration on *E. indica*

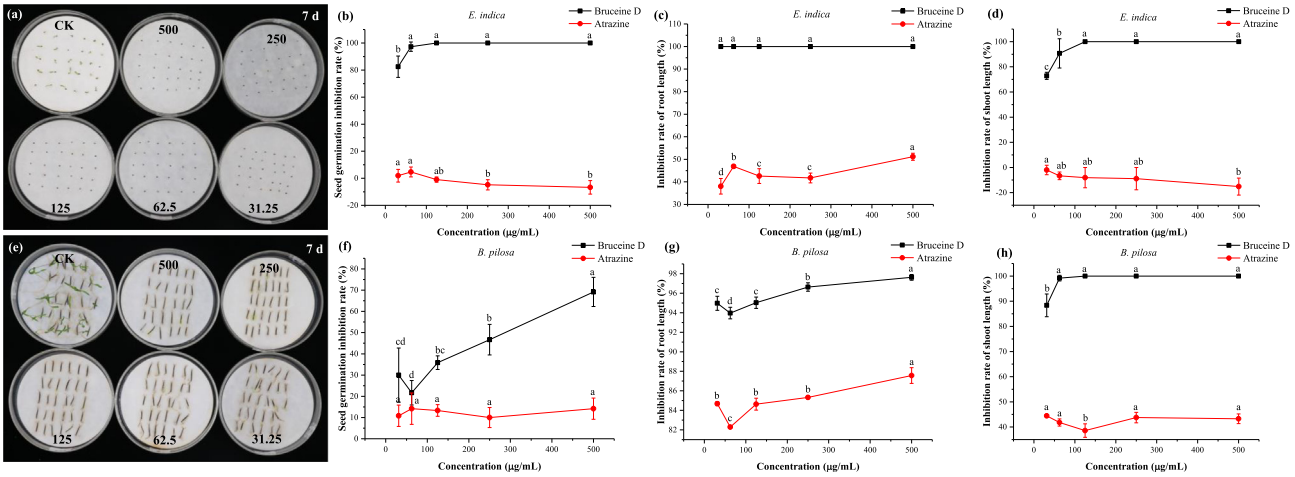

Fig. 5 Effects of different concentrations (31.25, 62.5, 125, 250 and 500 μg/mL) of bruceine D on *E. indica* (a) and *B. pilosa* (e). Effects of different concentrations of bruceine D on the seed germination (b), root (c) and shoot (d) length of *E. indica*. Effects of different concentrations of bruceine D on the seed germination (f), root (g) and shoot (h) length of *B. pilosa*. The data in the figure were given as mean ± SD for three repetitions. Different letters indicated significantly different ($p < 0.05$) at each same concentration, based on DMRT. (CK: negative control; Atrazine: positive control).

and *B. pilosa* were slightly different. At the concentration of 250 μg/mL, bruceine D had the strongest inhibitory effect on the seed germination of *E. indica* and the general inhibitory effect on the germination of *B. pilosa* seeds. However, bruceine E and F had a general inhibitory effect on the germination of *E. indica* seeds and very weak inhibitory effect on the seed germination of *B. pilosa*. By analyzing their structure–activity relationship (SAR), it can be concluded that the hydroxylation of ketone group at C-2 position is the main factor affecting their herbicidal activity, while the alkyl chain at C-13 position has no obvious effect on their herbicidal activity. The above results are similar to those of SAR of bruceines D–F in vitro anticomplement activity (Zhan et al., 2019). Therefore, the results of this study may provide a basis for further structure optimization of herbicide lead compounds and herbicides development with high efficiency and low toxicity.

At present, the research of *B. javanica* residue mainly focuses on its medical activities. For example, antitumor (Yan et al., 2019) and anti-inflammatory (Gao et al., 2019). However, there are still many active ingredients in the waste residue of *B. javanica* (Wang, 2016), which is necessary for its research and development. In this study, the herbicidal activity of *B. javanica* residue was systematically determined, and bruceine D, one of the active components from *B. javanica* residue, was determined. It not only makes full use of the waste resources of *B. javanica*, but also provides a foundation for its further application in agriculture.

5. Conclusion

The crude methanol extract, ethyl acetate extract and n-butanol extract of *B. javanica* residue have significant inhibitory effects on both *E. indica* and *B. pilosa*. Among them, n-butanol extract has the most significant inhibitory effect on the seed germination and growth of *E. indica*. Therefore, *B. javanica* residue can be used to control gramineous weeds in the field. At the same time, as a member of industrial Chinese medicine waste residue, *B. javanica* residue is used as organic fertilizer for weeding, realizing the real transformation of waste into treasure. In addition, bruceine D, E and F, isolated from the n-butanol extraction layer of *B. javanica* residue, have certain inhibitory activities against both *E. indica* and *B. pilosa*. In particular, bruceine D can significantly inhibit the germination of weed seeds at low concentrations. It has the potential to be used as a leading structure of herbicides for subsequent research and development, and has broad prospects for the control of gramineous weeds.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

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